510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
K032222

B. Analyte:
Helicobacter pylori antigens

C. Type of Test:
Lateral flow immunoassay

D. Applicant:
Meridian Bioscience Inc.

E. Proprietary and Established Names:
ImmunoCard STAT! HpSA

F. Regulatory Information:

1. Regulation section:
   21 CFR Part 866.3110 Campylobacter fetus serological reagents
2. Classification:
   Class I
3. Product Code:
   LYR – Campylobacter pylori
4. Panel:
   83 (Microbiology)

G. Intended Use:

1. Intended use(s):
   ImmunoCard STAT! HpSA is a rapid in vitro qualitative assay for the detection of Helicobacter pylori antigen (HpSA) in human stool. The stool antigen detection is intended to aid in the diagnosis of H. pylori infection and to demonstrate loss of H. pylori stool antigen following treatment. Conventional medical practice recommends that testing by any method to confirm the loss of antigen be done at least four weeks following completion of therapy.
2. Indication(s) for use:
   ImmunoCard STAT! HpSA is a rapid in vitro qualitative assay for the detection of Helicobacter pylori antigen (HpSA) in human stool. The stool antigen detection is intended to aid in the diagnosis of H. pylori infection and to demonstrate loss of H. pylori stool antigen following treatment. Conventional medical practice recommends that testing by any method to confirm the loss of antigen be done at least four weeks following completion of therapy.
3. Special condition for use statement(s):
   Not applicable
4. Special instrument Requirements:
   Not applicable

H. Device Description:

The ImmunoCard STAT HpSA is a rapid lateral flow immunoassay. It consists of chromatography strips impregnated with monoclonal anti-H. pylori as the capture antibody, red latex-conjugated detector antibody and blue latex-conjugated anti-protein as the detector antibodies for tests and controls respectively. Each strip is enclosed in a plastic frame with a window. The kit also contains positive control which is a dilute suspension of inactivated H. pylori in a buffered solution containing <0.1% sodium azide as a preservative as well as specimen diluent which is a buffered salt solution.

I. Substantial Equivalence Information:

1. Predicate device name(s):
   Premier Platinum HpSA
2. Predicate K number(s):
   K983255
3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended use	Detection of H.pylori antigen in stool	Detection of H.pylori antigen in stool
Assay	Qualitative	Qualitative
Specimen type	Stool	Stool
Differences		
Item	**Device**	**Predicate**
Technology	Lateral flow chromatography	Enzyme-linked immunoassay
Capture antibody	Monoclonal anti-H. pylori	Polyclonal anti-H. pylori
Conjugate	Red-latex conjugated anti-H. pylori	Rabbit polyclonal antibody specific for H. pylori conjugated to horse radish peroxidase
Result Interpretation	Visual read; end point visual color line	Results read by spectrophotometer; change in optical density of the solution

J. Standard/Guidance Document Referenced (if applicable):

FDA Guidance Document on H. pylori not referenced.

K. Test Principle:

Immuno*Card* STAT! HpSA uses capture solid phase technology to detect the presence of antigen in test specimens. To perform the test, patient stool is added to the Sample Diluent using the applicator stick that is part of the Sample Diluent Vial. The diluted stool sample (approximately a 1 in 10 dilution) is dispensed through the tip of the Sample Diluent Vial into the round sample window of the device. *H. pylori* antigen, if present in the diluted sample, binds to the detector antibody-latex conjugate as the sample moves through the device. The capture monoclonal antibody, which is bound to the assay membrane at reading window, binds the antigen-antibody-

latex complex and yields a visible pink-red line. When no antigen is present, no complex is formed and no pink-red line will appear at the test position of the central window.

A control line, appearing at the control position in the test window, shows whether adequate flow has occurred through the device during a test run. The control line is a protein of nonmammalian origin. Blue latex particles conjugated with a monoclonal antibody to this protein co-migrate with the latex-bound detector antibody during the incubation step. A blue line at the control position on the device should be present each time a specimen or control is tested. If no blue control line is seen, the test is considered invalid.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The reproducibility of ImmunoCard STAT! HpSA was determined with known negative (n = 5) and positive (n = 5) samples), that were coded and randomly sorted to prevent their identities. Two of the five positive samples were near the limit of detection for the assay. The reproducibility samples were tested on three consecutive days by three independent test sites. Intra-assay and interassay reproducibility was 100%.

			Referee (MBI)			Clinical Site # 1			Clinical Site # 2			Clinical Site # 3		
Sample Status	Premier OD reading	IC STAT! graded reading *	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day	Day 2	Day 3
Neg	0.017	0	0	0	0	0	0	0	0	0	0	0	0	0
Pos	0.737	4/5	+	+	+	+	+	+	+	+	+	+	+	+
Neg	0.016	0	0	0	0	0	0	0	0	0	0	0	0	0
Pos	1.140	7	+	+	+	+	+	+	+	+	+	+	+	+
Neg	0.028	0	0	0	0	0	0	0	0	0	0	0	0	0
Low Pos	1.442	1	+	+	+	w +	w +	w +	+	w +	+	+	+	+
Neg	0.042	0	0	0	0	0	0		0	0	0	0	0	0
Low Pos	1.041	2	+	+	+	+	w +	+	+	+	+	+	+	+
Pos	1.493	5	+	+	+	+	+	+	+	+	+	+	+	+
Neg	0.058	0	0	0	0	0	0	0	0	0	0	0	0	0
Pos Cont	2.309	N/A	+	+	+	+	+	+	+	+	+	+	+	+
Neg Cont	0.034	N/A	0	0	0	0	0	0	0	0	0	0	0	0

* The signal intensity (strength) of a positive reaction in ImmunoCard STAT! will not necessarily correlate with the OD value obtained in Premier Platinum HpSA EIA.

Legend: 0 = negative, 1-10 = semiquantitative scoring scale used in the interpretation of Immuno*Card* STAT! positive test results. (A value was assigned to the intensity of color in the Test Line, where 1 is the weakest visible positive reaction and 10 is the strongest. A 4/5 means the reaction fell between a grade of 4 and a grade of 5.) w = weak (correlates with a semiquantitative reaction grade of +/-, 1 or 2)

b. Linearity/assay reportable range:
Not applicable

c. Traceability (controls, calibrators, or method):
Not applicable

d. Detection limit:

The lower limit of detection of this assay is 64 ng/mL in tests with sonicated antigen prepared from *H. pylori* strain TV1970. This limit does not vary from formed (solid) to semi-solid stool.

e. Analytical specificity:

The specificity of Immuno*Card* STAT! HpSA was tested utilizing the following bacterial, viral and yeast strains. Positive and negative stools were spiked with $\geq 1 \times 10^8$ bacteria or yeast. None of the microorganisms tested yielded a positive result in the negative stool or interfered with detection of the positive stool. Both the negative and positive stool was positive when spiked with *Helicobacter pylori* strain 43504.

Adenovirus Type 2
Adenovirus Type 40
Coxsackie Type B1
Coxsackie Type B6
Echovirus Type 22
Feline calicivirus
Rotavirus
Aeromonas hydrophila
Campylobacter coli
Campylobacter jejuni
Candida albicans
Citrobacter freundii
Clostridium perfringens
Clostridium difficile (2)
Enterobacter cloacae
Enterococcus faecalis (2)
E. coli (2)
E. coli 0157:H7 (2)
E. fergusonii
Helicobacter felis
Klebsiella pneumoniae
Proteus vulgaris
Pseudomonas aeruginosa
Salmonella dublin
Salmonella (Group B)
Salmonella hilversum
Salmonella minnesota
Salmonella typhimurium
Staphylococcus aureus
Staphylococcus aureus (Cowan I)
Staphylococcus epidermidis
Serratia liquifaciens
Shigella boydii
Shigella dysenteriae
Shigella flexneri
Shigella sonnei
Yersinia enterocolitica

Borrelia burgdorferi (Stool inoculated with antigen protein to a final conc. of 32 ug/mL)

TESTS FOR INTERFERING SUBSTANCES
The following substances were found to have no effect on results when present in stool at the concentrations indicated.
Tums® Antiacid (5 mg/mL)
Tagamet® (5 mg/mL)
Prilosec® (5 mg/mL)
Mylanta® Antacid (1:20)
Pepto-Bismol® (1:20)
Barium sulfate (5%)
Whole Blood (50%)
Leukocytes (50%)
Mucin (3.4%)
Stearic acid/palmitic acid (fecal fat) (4%)
Hemoglobin (tarry stool) (12.5%)

f. Assay cut-off:

The assay cut off is 64 ng/ml of H.pylori antigen

2. Comparison studies:

a. Method comparison with predicate device:

Comparative studies: Four independent laboraories tested specimens in parallel with Immuno*Card* STAT! HpSA and a reference ELISA in vitro diagnostic method, Premier Platinum HpSA (Meridian Bioscience, Inc, Cincinnati, OH). Some samples giving discordant results between the two assays were sent to and evaluated by a reference laboratory. The results of the parallel tests are given below. Corrected results are calculated following investigation of discordant samples by the referee laboratory.

	Initial Trial Results	Corrected Results
Total samples tested	457	457*
Concordant test results	433	436
Positive samples	102	105
Negative samples	331	331
Discordant test results	21	20
Premier +, ImmunoCard -	6	6
Premier -, ImmunoCard +	15	14
Indeterminant	3	1
Premier Equivocal, ImmunoCard +	2	1
Premier Equivocal, ImmunoCard -	1	0
% correlation	95%	N/A

* Two discordant samples were QNS for follow up analysis.

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical sensitivity:

Clinical studies: Stool samples from 227 consecutive dyspeptic patients, who were not using acid suppressant therapy or antibiotics, and who were referred for endoscopy were tested with Immuno*Card* STAT! HpSA. Biopsy specimens were taken for histology, rapid urease test and culture. Patients were defined as infected with *H. pylori* if histology and urease tests were

positive, or if culture was positive. Eighty five of the 227 patients were found *H. pylori* positive. The results are summarized in the following table.

Diagnostic accuracy of Immuno*Card* STAT! HpSA before and after *H. pylori* eradication treatment.

	H. pylori status by endoscopy/biopsy/gold standard		
	True Positive	True Negative	Total
IC STAT! HpSA +	77	12	89
IC STAT! HpSA -	8	130	138
Total	85	142	227
Estimated clinical sensitivity (95% CI)	90.6% (84.9 to 97.1%)		
Estimated clinical specificity (95% CI)	91.5% (87.5 to 96.5%)		
Predictive value, positive test (95% CI)	86.5% (79.9 to 94.1%)		
Predictive value, negative test (95% CI)	94.2% (90.1 to 97.9%)		
Correlation (CI 95%)	91.2% (87.3 to 94.7%)		

Correlation of Immuno*Card* STAT! HpSA test results with eradication treatment

	H. pylori status by endoscopy/biopsy/gold standard		
	True Positive	True Negative	Total
IC STAT! HpSA +	21	0	21
IC STAT! HpSA -	1	63	64
Total	22	63	85
Estimated clinical sensitivity (95% CI)	95.4% (86.0 to 100%)		
Estimated clinical specificity (95% CI)	100%		
Predictive value, positive test (95% CI)	100%		
Predictive value, negative test (95% CI)	98.4% (94.5 to 100%)		
Correlation (CI 95%)	98.8% (96.8 to 100%)		

b. Clinical specificity:
Refer to (a) above

c. Other clinical supportive data (when a and b are not applicable):
Not applicable

4. Clinical cut-off:
   See assay cut off above
5. Expected values/Reference range:

Studies on the epidemiology of *H. pylori* have shown that this organism is present worldwide. Gastritis caused by *H. pylori* has been shown to correlate with age, ethnic background, family size and socioeconomic class. The prevalence of *H. pylori* infection in a given population can vary from 20% to 90%. In patients diagnosed with duodenal ulcers, however, it has been shown in every age group to be approximately 80%. Currently recommended eradication treatments have an efficacy rate between 75% and 90%.

The Immuno*Card* STAT! HpSA test detects the presence of *H. pylori* antigens in human stool. Expected values for a given population should be determined for each laboratory. The rate of positives may vary depending on geographic location, method of specimen collection, handling and transportation, test employed and general health environment of patient population under study.

M. Conclusion:

The ImmunoCard STAT! HpSA is substantially equivalent in performance to the predicate device for the detection of Helicobacter pylori antigen in human stool.